TURKISH JOURNAL OF EMERGENCY MEDICINE

Original Article

Access this article online

Quick Response Code:

Website: https://turkjemergmed.com/

DOI: 10.4103/tjem.tjem_36_25

Sepsis-induced coagulopathy and its association with mortality in patients with sepsis and septic shock

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Abstract:

OBJECTIVES: Sepsis-induced coagulopathy (SIC) is a common complication in patients with sepsis and septic shock. Early detection of SIC is crucial for timely intervention, as it can significantly impact patient outcomes. This study aims to evaluate the prevalence of SIC and its impact on the 28-day mortality rate in patients with sepsis and septic shock.

METHODS: A single-center retrospective observational cohort study was conducted in Vietnam from January 2021 to August 2024. Adult patients diagnosed with sepsis or septic shock who were admitted to the intensive care unit within 24 h of initial presentation were included. Patients with do-not-resuscitate orders, coagulopathy, malignant blood disorders, incomplete data, or refusal of treatment were excluded. SIC scores were assessed, and 28-day mortality rates were recorded.

RESULTS: A total of 340 patients were included, with 216 (63.5%) exhibiting SIC (SIC score ≥4). The mean age of patients was 69.01 ± 17.04 years, and the majority were male (61.5%). Septic shock accounted for 79.7% of the cases. SIC patients had significantly higher mortality rates at both 4 days (17.6% vs. 4.8%, $P = 0.001$) and 28 days (40.3% vs. 24.4%, $P = 0.005$). Nonsurvivors exhibited higher SIC (73.9% vs. 57.9%, $P = 0.003$) and had worse disease severity scores. Multivariate analysis confirmed that SIC score ≥4 was strongly associated with increased 28-day mortality (odds ratio 1.799, $P = 0.033$).

CONCLUSIONS: The prevalence of SIC is high in patients with sepsis and septic shock, especially in our cohorts. SIC score ≥4 is also a strong and independent predictor for 28-day mortality.

Keywords:

Coagulopathy, mortality, sepsis, septic shock

Submitted: 28-01-2025
Revised: 13-06-2025
Accepted: 01-07-2025
Published: 01-01-2026

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Introduction

Sepsis is a critical condition defined by life-threatening organ dysfunction caused by an aberrant host response to infection. Sepsis can lead to multiorgan dysfunction, with shock and severe coagulopathy being among the most common complications.[1] Coagulation abnormalities encompass a broad spectrum of clinical symptoms, ranging from mild hemostatic abnormalities, such as a slight reduction in platelet amount, to severe conditions like disseminated intravascular coagulation (DIC).[2] The DIC in sepsis is characterized by an acute systemic inflammatory reaction resulting in endothelial dysfunction, coagulation disturbance induced by the infection, and other etiologies. The subsequent inflammatory response significantly influences patient outcomes.[3] For the diagnosis of overt DIC, the International Society on Thrombosis and Hemostasis (ISTH) created the DIC score.[4]

How to cite this article: Quy HP, Thoi NT, Thanh NH, Hai PD. Sepsis-induced coagulopathy and its association with mortality in patients with sepsis and septic shock. Turk J Emerg Med 2026;26:28-36.

Box-ED Section

What is already known on the study topic?

- Sepsis can lead to multi-organ dysfunction, with shock and severe coagulopathy being among the most common complications
- It is widely recognized that overt disseminated intravascular coagulation is primarily a late complication of sepsis.

What is the conflict on the issue? Is it important for readers?

- It is crucial for the early detection of patients with sepsis-associated coagulopathy before they reach the stage of severe hemostatic derangement, which facilitates the new score, known as the SIC (Sepsis-Induced Coagulopathy) score
- There are few studies to investigate SIC, and the outcomes and incidences of positive SIC vary across different cohorts, particularly within the Asian population, excluding Japanese cohorts.

How is this study structured?

- This is a single-center, retrospective, observational cohort study conducted in 340 patients.

What does this study tell us?

- The prevalence of SIC is higher in our population than in other cohorts
- SIC score ≥4 is also an independent predictor for 28-day mortality.

However, overt DIC is generally a late-stage complication of sepsis, and the ISTH DIC score, based on strict criteria, may delay opportunities for early intervention.[5]

It is crucial for the early detection of patients with sepsis-associated coagulopathy before they reach the stage of severe hemostatic derangement. This is the rationale for the Scientific and Standardization Committee on DIC of ISTH proposed a new score, known as the Sepsis-induced coagulopathy (SIC) score, which aims to detect DIC early on.[6] The concept of "infection-induced organ dysfunction and coagulopathy" facilitates SIC diagnostic criteria, which include platelet count, the Sequential Organ Failure Assessment (SOFA) score, and prothrombin time (PT; international normalized ratio [INR]).[7] A SIC score ≥ 4 indicates significant coagulopathy associated with increased risk of adverse outcomes. Other studies have sought to validate the utility of the recently proposed SIC score in determining the timing of diagnosis, predicting mortality, and guiding the initiation of anticoagulant therapy in the adult population.[6,8] In Japan, the population with SIC score was selected strictly by criteria of severe sepsis and DIC according to the criteria of the Japanese Ministry of Health.[9,10] Furthermore, around one-half of patients with suspected DIC were treated with at least one of the antithrombin and thrombomodulin drugs.[6,11] Therefore, it remains uncertain whether the outcomes and incidences vary across different cohorts, particularly within the Asian population, excluding Japanese cohorts. This study aims to evaluate the prevalence of coagulation disorders using the SIC score and its association with 28-day mortality in patients with sepsis and septic shock.

Methods

Study population

This is a single-center, retrospective, observational cohort study conducted at a tertiary hospital in Vietnam from January 1st, 2021, to August 31st, 2024. Ethics Committee of the 108 Military Central Hospital approved this study with document reference number 2757/GCN – BV on May 10, 2024. We included adult patients diagnosed with sepsis or septic shock and admitted to the intensive care unit (ICU) within 24 h of onset [Figure 1]. Sepsis and septic shock diagnoses were based on Sepsis-3 definitions.[1] Patients were excluded if they met any of the following criteria: (1) Do Not Resuscitate orders; (2) history of coagulopathy or malignant blood disorders; (3) use of medications that affect coagulation; (4) incomplete clinical or laboratory data; or (5) refusal of treatment.

Data collection

Clinical and laboratory data were collected from the hospital's electronic medical records of patients at hospital admission. These included baseline demographic information, comorbidities, and vital signs at admission. Laboratory data included a complete blood count, comprehensive metabolic panel, and coagulation parameters such as fibrinogen, INR, PT, activated partial thromboplastin time (aPTT), and D-dimer.

Illness severity was evaluated within 24 h of ICU admission using the SOFA score,[12] Acute Physiology and Chronic Health Evaluation II score (APACHE II),[13] and Simplified Acute Physiology Score II (SAPS II).[14]

In our study, we completely excluded patients with incomplete data regarding the key parameters needed for SIC scoring (platelet count, PT/INR, and SOFA score). We applied a complete case analysis approach and did not perform imputations for missing data.

Coagulation assessment

SIC was calculated on ICU admission (day 0) using published criteria.[9] The SIC score includes platelet count, SOFA score, and PT/INR. A SIC score ≥4 was considered positive. The ISTH criteria were also used to assess the presence of overt DIC, with D-dimer thresholds set at ≥5000 ng/mL for a severe increase and ≥2000 ng/mL for a moderate increase.[15]

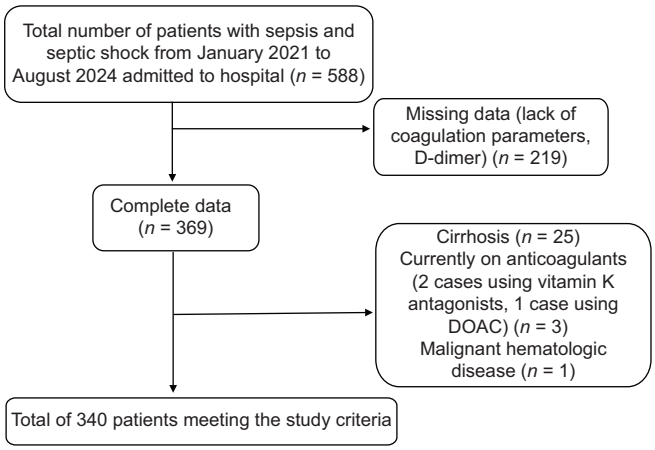

Figure 1: Study cohort enrollment flowchart

Study outcomes

The primary outcome was the prevalence of the SIC score in patients with sepsis and septic shock. The secondary outcome assessed the association between SIC at admission and the 28-day mortality rate.

Statistical analysis

SPSS version 29 (Hearne Scientific Software Pty Ltd, New South Wales, Australia) was used for statistical analyses. We characterized data distribution using standard methods: In normally distributed data, continuous variables were expressed as mean ± standard deviation, while in nonnormal distributions, these variables were presented as median with interquartile range. In contrast, categorical variables were presented as absolute numbers and proportional percentages. Between-group comparisons employed Chi-squared or Fisher's exact tests for categorical data. In contrast, independent *t*-tests or Mann–Whitney *U*-tests were used to analyze continuous variables, depending on the data distribution. P <0.05 was statistically significant.

Results

Characteristics of the study group based on sepsis-induced coagulopathy score

Baseline characteristics of the study population

A total of 340 patients were included in the study, with 216 patients (63.5%) having a SIC score ≥4. The mean age was 69.01 ± 17.04 years, and the majority were male (61.5%). Septic shock accounted for 79.7% of the cases. No significant differences were observed in baseline characteristics, including the proportion of septic shock, mechanical ventilation, heart rate, mean arterial pressure, norepinephrine dosage, use of continuous renal replacement therapy (CRRT), infection source, or disease severity scores (APACHE II, SOFA, SAPS 2) between the SIC and non-SIC groups. However, significant differences were found in gender distribution (males: 57.4% vs. 68.5%, P = 0.042) and the prevalence of coronary artery disease (4.2% vs. 10.5%, P = 0.023). Patients with SIC had significantly higher mortality rates at both 4 days (17.6% vs. 4.8%, P = 0.001) and 28 days (40.3% vs. 24.4%, P = 0.005) [Table 1].

Laboratory findings

Apart from the laboratory results that are components of the SIC score (platelet count, PT, and aPTT), the majority of results did not show statistically significant differences between the groups with and without SIC (SIC ≥4 vs. SIC <4). Serum creatinine, hemoglobin levels, and electrolyte profiles showed no significant differences between the two groups. Procalcitonin (20.1 [3.4–75.8] vs. 8.4 [1.6–52.7] ng/mL, P = 0.009) and lactate level (3.8 [2.2–6.1] vs. 2.9 [1.5-4.6] mmol/L, P = 0.004) were significantly higher in the SIC group. SIC patients exhibited higher total serum bilirubin levels (19 [11–38] vs. 12 [8–20] μmol/L, P < 0.001) and AST levels (66 [22–113] vs. 34 [19–60] U/L, P = 0.002).

Comparison of clinical characteristics between 28-day survivors and nonsurvivors patient characteristics

Among 340 patients, 221 (65%) survived, and 119 (35%) died at 28 days. Nonsurvivors demonstrated higher rates of mechanical ventilation (93.3% vs. 65.2%, P < 0.001). The duration of mechanical ventilation was significantly longer in nonsurvivors (6.7 [5.5–7.8] vs 5.7 [4.5–6.8] days, P < 0.001). CRRT was more frequently required in nonsurvivors (70.6% vs. 56.7%, P < 0.001), with higher norepinephrine requirements (0.33 [0.10–0.75] vs. 0.16 [0.07–0.35] μg/kg/min, P < 0.001).

Regarding comorbidities, chronic kidney disease (17.6% vs. 10.0%, P = 0.042) and cardiac arrest (8.4% vs. 2.7%, P = 0.018) were more prevalent in nonsurvivors. The primary source of infection differed significantly between groups, with higher rates of pulmonary (58.8% vs. 47.1%, P = 0.038) and urinary tract infections (2.5% vs. 15.8%, P < 0.001) in nonsurvivors [Table 2].

Laboratory findings and disease severity

Laboratory parameters showed distinct patterns between groups. Nonsurvivors had lower red blood cell counts (3.8 [3.1–4.3] vs. 4.1 [3.5–4.6] $\times 10^{12}$/L, P = 0.026) and prolonged aPTT (36.4 [30.0–43.2] vs. 34.2 [29.7–38.9] s, P = 0.039). Disease severity scores were consistently higher in nonsurvivors, including SOFA (12 [9–15] vs. 9 [7–11]), SAPS-II (48 [38–60] vs. 40 [28–49]), APACHE II (22 [19–28] vs. 18 [14–24]), and mNUTRIC scores (6 [4–7] vs. 5 [3–6]), P < 0.001 [Table 2].

Clinical outcomes

SIC scores ≥4 were more prevalent in nonsurvivors (73.9% vs. 57.9%, P = 0.003). In our cohort, 63.5% of patients (216/340) had a SIC score ≥4, and the overall

Table 1: Baseline characteristics of the study group according to sepsis-induced coagulopathy score

Background	Total (*n*=340)	SIC ≥4 (*n*=216)	SIC <4 (*n*=124)	*P*
Age (years)	69.01±17.04	69.65±17.27	67.89±16.63	0.430
Male, *n* (%)	209 (61.5)	124 (57.4)	85 (68.5)	0.042
Length of hospital stay (days)	13 (8–22)	14 (7–24)	13 (8–19)	0.573
Length of ICU stay (days)	7 (3–13)	7 (3–13)	7 (4–13)	0.760
Day of MV (days)	3.5 (1.0–8.0)	3.0 (1.0–8.0)	4.0 (0.2–8.0)	0.942
MV, *n* (%)	255 (75)	162 (75)	93 (75)	1.000
CRRT, *n* (%)	165 (48.5)	107 (49.5)	58 (46.8)	0.624
Pulse (bpm)	110 (90–122)	110 (95–125)	105 (90–120)	0.120
MAP (mmHg)	78.3 (70.0–88.3)	80.0 (70.0–88.3)	76.6 (70.0–86.6)	0.198
Noradrenalin dose (µg/kg/min)	0.20 (0.07–0.49)	0.21 (0.07–0.50)	0.15 (0.02–0.41)	0.124
Concomitant comorbidities, *n* (%)				
Coronary disease	22 (6.5)	9 (4.2)	13 (10.5)	0.023
Hypertension	182 (53.5)	109 (50.5)	73 (58.9)	0.135
Heart failure	32 (9.4)	21 (9.7)	11 (8.6)	0.796
TIA/stroke	60 (17.6)	32 (14.8)	28 (22.6)	0.071
COPD	31 (9.1)	21 (9.7)	10 (8.1)	0.609
Diabetes	110 (32.4)	64 (29.6)	46 (37.1)	0.157
CKD	43 (12.6)	32 (14.8)	11 (8.9)	0.112
Alcoholic	16 (4.7)	11 (5.1)	5 (4.0)	0.657
Cancer	30 (8.8)	23 (10.6)	7 (5.6)	0.117
Cardiac arrest	16 (4.7)	10 (4.6)	6 (4.8)	0.930
Smoking	22 (6.5)	15 (6.9)	7 (5.6)	0.639
Infection origin, *n* (%)				
Pulmonary	175 (51.2)	111 (50.9)	64 (51.6)	0.900
Abdomen	83 (24.4)	49 (22.7)	34 (27.4)	0.328
Urinary	38 (11.2)	23 (10.6)	15 (12.1)	0.680
Skin	17 (5.0)	14 (6.5)	3 (2.4)	0.090
Other	27 (7.9)	19 (8.8)	8 (6.5)	0.440
Laboratory parameters				
Hemoglobin (g/L)	119 (104–135)	118 (100–133)	125 (104–140)	0.072
RBC ($\times10^{12}$/L)	4.0 (3.4–4.5)	3.8 (3.3–4.4)	4.2 (3.5–4.7)	0.02
Hematocrit (%)	36 (31–41)	36 (31–41)	38 (33–43)	0.071
WBC ($\times10^{9}$/L)	14.0 (8.3–20.4) 16.1	12.9 (8.2–20.0)	15.1 (9.4–20.7)	0.315
Neutrophil ($\times10^{9}$/L)	11.7 (6.9–17.5)	11.0 (6.1–17.4)	12.7 (7.9–17.9)	0.333
aPTT (s)	35.0 (29.8–39.7)	36.5 (30.7–42.3)	32.4 (28.4–36.4)	< 0.001
Fibrinogen (g/L)	4.6 (3.6–5.6)	4.5 (3.5–5.6)	4.6 (3.7–5.5)	0.890
D-Dimer (ng/mL)	5882 (2744–7012)	6550 (3141–7129)	5204 (2437–7012)	0.065
Ure (mmoL/L)	11.7 (8.0–17.9)	12.0 (8.1–17.8)	11,2 (7.4–17.9)	0.420
Creatinine (µmoL/L)	152 (98.3–262.0)	157 (101.0–262.0)	131 (91.7–262.0)	0.400
AST (U/L)	61 (36–156)	72 (41–231)	48 (27–90)	< 0.001
ALT (U/L)	40 (21–91)	46 (22–113)	34 (19–60)	0.002
Bilirubin total (µmoL/L)	16 (10–28)	19 (11–38)	12 (8–20)	< 0.001
Bilirubin direct (µmoL/L)	6 (3–16)	7 (3–24)	4 (2–7)	< 0.001
Glucose (mmoL/L)	8.8 (6.3–14.0)	8.6 (6.4–13.7)	9.6 (7.0–14.2)	0.037
Na (mmoL/L)	137 (134–141)	137 (133–142)	137 (133–141)	0.648
K (mmoL/L)	3.9 (3.4–4.6)	3.9 (3.4–4.6)	4.1 (3.5–4.8)	0.336
Cl (mmoL/L)	103 (99–108)	102 (99–109)	103 (99–107)	0.697
Mg (mmoL/L)	0.75 (0.62–0.90)	0.75 (0.60–0.89)	0.75 (0.62–0.89)	0.394
Protein (g/L)	58.0 (51.1–65.0)	56.9 (50.6–63.0)	60.4 (54.7–66.0)	0.004
Albumin (g/L)	29.0 (25.6–32.3)	28.7 (25.4–31.5)	30.0 (26.0–34.1)	0.030
CRP (mg/dL)	139 (77–218)	164 (81–246)	123 (73–173)	0.034
Procalcitonin (ng/mL)	15.5 (2.6–68.4)	20.1 (3.4–75.8)	8.4 (1.6–52.7)	0.009
Lactate (mmoL/L)	3.5 (2.0–5.7)	3.6 (2.2–6.1)	2.9 (1.5–4.6)	0.004
Severity score				
SOFA	10 (8–13)	11 (8–14)	9 (7–11)	0.210

Contd...

Table 1: Contd...

Background	Total (*n*=340)	SIC ≥4 (*n*=216)	SIC <4 (*n*=124)	*P*
SAPS II	43 (32–53)	43 (33–54)	42 (30–52)	0.350
APACHE II	20 (15–26)	20 (15–25)	19 (15–26)	0.520
mNUTRIC	5 (4–6)	5 (4–6)	5 (4–6)	0.910
Endpoints, *n* (%)				
Septic shock	271 (79.7)	176 (81.5)	95 (76.6)	0.283
4 days mortality	44 (12.9)	38 (17.6)	6 (4.8)	0.001
28 days mortality	117 (34.5)	87 (40.3)	30 (24.4)	0.003
In hospital mortality	134 (39.4)	88 (40.7)	46 (37.1)	0.510

MV: Mechanical ventilation, CRRT: Continuous renal replacement therapy, MAP: Mean arterial pressure, COPD: Chronic obstructive pulmonary disease, TIA: Transient ischemic attack, CKD: Chronic kidney disease, RBC: Red blood cell, WBC: White blood cell, aPTT: Activated partial thromboplastin time, ALT: Alanine transaminase, AST: Aspartate transaminase, CRP: C-reactive protein, SOFA: Sequential organ failure assessment, SAPS II: Simplified acute physiology score II, APACHE II: Acute Physiology and Chronic Health Evaluation II, mNUTRIC Score: Modified nutrition risk in critically Ill, DIC: Disseminated intravascular coagulation, SIC: Sepsis-induced coagulopathy, ICU: Intensive care unit

28-day mortality rate was 34.5% (117/340). Univariate analysis revealed several predictors of increased mortality risk. Mechanical ventilation was the most significant, with a 7.41-fold increase in mortality risk (95% confidence interval [CI]: 3.450–16.670, $P < 0.001$), followed by the need for noradrenaline (2.84-fold, 95% CI 2.088–7.129, $P < 0.001$) and CRRT (4.15-fold, 95% CI: 2.360–6.670, $P < 0.001$). Cardiac arrest and pulmonary infection also significantly raised the risk of death, with odds ratios (OR) of 3.35-fold (95% CI: 1.180–9.434, $P = 0.023$) and 1.66-fold (95% CI: 1.053–2.597, $P = 0.004$), respectively. A SIC score of 4 or more was another predictor, with a 2.06-fold increase in mortality risk (95% CI: 1.260–3.360, $P = 0.004$).

In the multivariate analysis, after adjusting for potential confounders, mechanical ventilation remained the strongest independent predictor (OR 5.085, 95% CI: 2.140–13.698, $P < 0.001$), followed by noradrenaline requirements (OR 2.280, 95% CI: 1.231–4.223, $P = 0.009$). Among clinical factors, a urinary source of infection was protective, reducing mortality risk (OR 0.230, 95% CI: 0.087–0.764, $P = 0.029$). In addition, a SIC score ≥4 nearly doubled the risk of death (OR 1.799, 95% CI 1.384–2.242, $P = 0.033$), and each point increase in the SOFA score was associated with a higher risk of mortality (OR 1.086, 95% CI: 1.014–1.165, $P = 0.019$) [Table 3].

Discussion

SIC is a critical factor in the pathophysiology of sepsis and septic shock, representing an early stage of coagulation dysfunction before overt DIC manifests. This study highlights the prevalence of SIC and its association with 28-day mortality in patients with sepsis and septic shock, emphasizing the utility of the SIC score as an early diagnostic tool. In this study, 63.5% of patients with sepsis and septic shock had a SIC score ≥ 4, reflecting a high burden of coagulopathy in this critically ill population.

The clinical profiles in Table 2, including higher use of organ support (mechanical ventilation, CRRT, and vasopressors) and worse severity scores (SOFA, SAPS II, and APACHE II) among nonsurvivors, confirm that SIC ≥4 aligns closely with overall clinical deterioration. This supports its utility as a prognostic marker, complementing traditional severity scoring systems. Moreover, the length of hospital stay was longer in survivors compared to nonsurvivors (14 vs. 8 days, $P < 0.001$). This can be explained by the fact that hospitalization for nonsurvivors ends at the time of death, whereas survivors tend to require a longer stay for the recovery process. It is important to distinguish SIC from the ISTH DIC score. While both share platelet count and PT/INR as components, the SIC score excludes fibrinogen and D-dimer, focusing instead on early detection by incorporating the SOFA score to reflect concurrent organ dysfunction. This design enhances its utility for identifying coagulopathy earlier in the sepsis continuum. In our multivariate analysis, SIC score ≥4 remained an independent predictor of 28-day mortality (OR 1.799, $P = 0.033$), even after adjusting for SOFA and other clinical variables.

Sepsis is a dysregulated host response to infection characterized by an inflammatory process. The inflammatory response is triggered by recognizing pathogen-associated molecular patterns in immune cells.[16] Robust platelet activation contributes to the high incidence of thrombocytopenia observed in sepsis, ranging from 37.5% to 83.5%.[17,18] Tissue factor released from damaged epithelium can activate the coagulation cascades. The tissue factor has long been proven to be a key factor in initiating the extrinsic coagulation cascade and the subsequent formation of thrombosis.[19] Neutrophil extracellular traps, released by activated neutrophils, have vigorously promoted hypercoagulability in inflammation and significantly contributed to the incidence and mortality of SIC.[3,11,20,21] In summary, in sepsis, the body's immune response triggers a state of hypercoagulation, leading to the

Table 2: Comparison of clinical characteristics between 28-day survivors and nonsurvivors in patients with sepsis and septic shock

Background	Survivors (*n*=221)	Nonsurvivors (*n*=119)	*P*
Age (years)	70.0±9.5	72.0±13.0	0.230
Male, *n* (%)	133 (60.2)	76 (63.9)	0.500
Septic shock, *n* (%)	175 (78.8)	96 (81.4)	0.581
MV, *n* (%)	144 (65.2)	111 (93.3)	<0.001
Day of MV (days)	5.7 (4.5–6.8)	6.7 (5.5–7.8)	<0.001
CRRT, *n* (%)	81 (36.7)	84 (70.6)	<0.001
Pulse (bpm)	105 (90–120)	115 (100–130)	0.500
MAP (mmHg)	79.6 (70.0–88.5)	76.6 (70.0–86.6)	0.200
Noradrenalin dose (µg/kg/min)	0.16 (0.07–0.35)	0.33 (0.10–0.75)	<0.001
Length of hospital stay (days)	14 (10–23)	8 (4–20)	<0.001
Length of ICU stay (days)	8.0±4.5	6.0±4.5	0.170
Concomitant comorbidities, *n* (%)			
Coronary disease	15 (6.8)	7 (5.9)	0.750
Hypertension	120 (54.3)	62 (52.1)	0.690
Heart failure	20 (9.0)	12 (10.1)	0.750
TIA/stroke	41 (18.6)	19 (16.0)	0.550
COPD	18 (8.1)	13 (10.9)	0.390
Diabetes	72 (32.6)	38 (31.9)	0.900
CKD	22 (10.0)	21 (17.6)	0.042
Alcoholic	9 (4.1)	7 (5.9)	0.450
Cancer	13 (5.9)	17 (14.3)	0.009
Cardiac arrest	6 (2.7)	10 (8.4)	0.018
Smoking	11 (5.0)	11 (9.2)	0.120
Infection origin, *n* (%)			
Pulmonary	104 (47.1)	70 (58.8)	0.038
Abdomen	52 (23.5)	31 (26.1)	0.600
Urinary	35 (15.8)	3 (2.5)	<0.001
Skin	10 (4.5)	7 (5.9)	0.580
Other	19 (8.6)	8 (6.7)	0.540
Laboratory parameters			
Hemoglobin (g/L)	121 (103–136)	116 (96–132)	0.200
RBC ($\times10^{12}$/L)	4.1 (3.5–4.6)	3.8 (3.1–4.3)	0.026
Hematocrit (%)	37 (32–42)	35 (30–41)	0.076
WBC ($\times10^{9}$/L)	14.4 (8.3–20.4)	12 (8.2–20.3)	0.260
Neutrophil ($\times10^{9}$/L)	13.1 (7.1–17.5)	10.7 (6.9–17.4)	0.438
Platelets ($\times10^{9}$/L)	179 (114–182)	158 (85–252)	0.390
PT (%)	72.0 (61.0–89.0)	72.0 (55.0–86.0)	0.610
aPTT (s)	34.3 (29.7–38.9)	36.4 (30.1–43.2)	0.039
INR	1.23 (1.08–1.43)	1.3 (1.11–1.54)	0.320
Fibrinogen (mg/dL)	4.6 (3.7–5.7)	4.5 (3.4–5.5)	0.490
D-Dimer (ng/mL)	6060 (2727–7408)	5595 (2957–7000)	0.550
Ure (mmoL/L)	11.7 (8.0–17.7)	12.0 (7.9–19.0)	0.610
Creatinine (µmoL/L)	149 (97.5–267.5)	157.0 (106.0–237.5)	0.410
AST (U/L)	57.0 (32.4–104.0)	71.5 (42.2–229.0)	0.410
ALT (U/L)	38.0 (20.0–85.1)	43.3 (23.0–110.0)	0.330
Bilirubin total (µmoL/L)	15.0 (9.7–26.0)	15.5 (10.9–29.6)	0.488
Bilirubin direct (µmoL/L)	5.6 (2.6–13.5)	6.0 (3.5–18.7)	0.033
Glucose (mmoL/L)	9.1 (6.4–14.1)	9.0 (7.0–13.4)	0.980
Na (mmoL/L)	138 (134–142)	136 (131–140)	0.737
K (mmoL/L)	3.9 (3.4–4.6)	4.2 (3.6–4.8)	0.053
Cl (mmoL/L)	103 (99–108)	102 (99–107)	0.728
Mg (mmoL/L)	0.76 (0.62–0.90)	0.74 (0.59–0.85)	0.804
Protein (g/L)	58.2 (53.3–65.0)	57.2 (50.2–65.0)	0.540
Albumin (g/L)	29.0 (26.0–33.0)	28.2 (25.3–31.7)	0.590

Contd...

Table 2: Contd...

Background	Survivors (*n*=221)	Nonsurvivors (*n*=119)	*P*
CRP (mg/dL)	139.5 (80.0–221.8)	134.0 (69.6–197.9)	0.380
Procalcitonin (ng/mL)	17.5 (2.31–65.1)	13.6 (2.8–69.4)	0.460
Lactate (mmoL/L)	3.35 (1.90–5.38)	3.45 (1.95–5.08)	0.329
Score			
SIC ≥4, *n* (%)	128 (57.9)	88 (73.9)	0.003
SOFA	9 (7–11)	12 (9–15)	<0.001
SAPS II	40 (29–49)	48 (38–60)	<0.001
APACHE II	18 (14–24)	22 (19–28)	<0.001
mNUTRIC	5 (3–6)	6 (4–7)	<0.001
DIC	3 (3–4)	4 (3–5)	0.018

MV: Mechanical ventilation, CRRT: Continuous renal replacement therapy, MAP: Mean arterial pressure, COPD: Chronic obstructive pulmonary disease, TIA: Transient ischemic attack, CKD: Chronic kidney disease, RBC: Red blood cell, WBC: White blood cell, PT: Prothrombin time, aPTT: Activated partial thromboplastin time, INR: International normalized ratio, ALT: Alanine transaminase, AST: Aspartate transaminase, CRP: C-reactive protein, SOFA: Sequential organ failure assessment, SAPS II: Simplified acute physiology score II, APACHE II: Acute Physiology and Chronic Health Evaluation II, mNUTRIC Score: Modified nutrition risk in critically Ill, DIC: Disseminated intravascular coagulation, SIC: Sepsis-induced coagulopathy, ICU: Intensive care unit

Table 3: Univariate and multivariate logistic regression analysis of clinical factors associated with 28-day mortality in sepsis and septic shock

	Univariate analysis			Multivariate analysis		
	OR	95% CI	*P*	OR	95% CI	*P*
MV	7.410	3.450–16.670	<0.001	5.085	2.140–13.698	<0.001
Noradrenalin dose (μg/kg/min)	3.858	2.088–7.129	<0.001	2.280	1.231–4.223	0.009
Pulmonary infection	1.656	1.053–2.597	0.604			
Urinary infection	0.139	0.042–0.464	0.001	0.230	0.087–0.764	0.029
aPTT (s)	1.002	0.995–1.009	0.616			
SIC score ≥4	2.060	1.260–3.360	0.004	1.799	1.384–2.242	0.033
SOFA	1.180	1.100–1.250	<0.001	1.086	1.014–1.165	0.019
DIC	1.234	1.029–1.480	0.023			

MV: Mechanical ventilation, SOFA: Sequential organ failure assessment, SIC: Sepsis-induced coagulopathy, DIC: Disseminated intravascular coagulation, aPTT: Activated partial thromboplastin time, OR: Odds ratio, CI: Confidence interval

formation of thrombi and inhibition of thrombolysis factors contributing to the pathogenesis of sepsis, such as the nature and degree of pathogen invasion and the host immune response, are also central to determining the pathogenesis and severity of coagulopathy.

When compared with findings from current data from previous studies, our result revealed both areas of agreement and divergence, offering a deeper understanding of coagulopathy in sepsis patients. Among recent high-quality research addressing this topic, the HYPRESS trial was a double-blind randomized controlled trial conducted across 34 centers in Germany, involving prospective data from 380 sepsis patients.[22] Newly published in June 2024, a retrospective observational cohort study by Tullo collected 357 cases of sepsis diagnosed in the ED to evaluate the predictive value of the SIC score in sepsis outcomes.[23] We observed a significantly higher prevalence of coagulopathy, defined as SIC ≥4, in our sepsis patients (63.5%) compared to the HYPRESS trial (22.1%) and study by Tullo *et al*. (15.4%).[8,22,23] Meanwhile, compared to the classical report on SIC first introduced by Iba *et al*., the prevalence of SIC among patients diagnosed with sepsis in our study is comparable (63.5% vs. 60.2%).[9] The high SIC prevalence in our study (63.5%) compared to Western cohorts (15.4%–22.1%) can be explained by several key factors. As noted, the first two studies mainly collected data from patients in emergency departments or intermediate care units, whereas our study and that of Iba *et al*. primarily focused on patients in the ICU, where conditions are typically more critical. This discrepancy underscores the significantly high prevalence of coagulopathy in patients with sepsis admitted to the ICU. Furthermore, as a tertiary referral center in Vietnam, our hospital receives the most severe cases from lower-level facilities, resulting in a concentration of advanced sepsis patients. The delayed healthcare presentation, common in our setting, allows unchecked progression of sepsis before intervention. Our assessment of SIC within 24 h of ICU admission likely captures peak coagulation derangements. In addition, the predominance of pulmonary infections (51.2%) in our cohort may contribute to different coagulation patterns compared to other populations. Furthermore, due to differences in the selection of study populations, the mortality rates in patients with sepsis and SIC vary significantly. The 28-day mortality in patients admitted to the ICU is markedly higher (40.3% in our study and 38.4% in Iba research) compared to other studies, which

report mortality rates ranging from 17.2% to 26.8%.[9,22,23] The similarity across all listed studies is that SIC ≥4 is a positive prognostic factor for 28-day mortality in the study populations. A significantly higher mortality rate over 28 days was observed in patients with SIC in our study and in the re-analysis of the HYPRESS trial and the study by Schmoch or Iba *et al*.[8,9] Highlighted in Tullo's study, SIC ≥4 is an independent predictor of 28-day mortality with an OR of 2.28 (1.16–4.48) and a $P = 0.017$. Prolonged aPTT is significantly more common in nonsurviving patients across the studies.[23] Other research reveals that SIC typically occurs during diagnosis or within the first 4 days.[9,22,24] Tullo *et al*. also reported a significant correlation between SIC ≥4 and the development of DIC, new organ damage, bleeding, thrombosis, and the need for transfusion.[23]

Based on our findings, we propose four key clinical applications for SIC scoring: First, as an initial screening tool in emergency departments using readily available parameters to quickly identify high-risk patients, particularly in resource-limited settings. Second, for risk stratification and ICU admission decisions, patients with SIC ≥4 showed significantly higher mortality rates (40.3% vs. 24.4% at 28 days). Third, for guiding monitoring frequency – daily assessments for SIC <4 and for SIC ≥4 during the first 72 h. Fourth, to identify patients who may benefit from targeted interventions, including closer monitoring for thrombotic/bleeding complications, more aggressive source control, and cautious transfusion strategies. Given the strong association between SIC and mortality (OR 1.799), implementing SIC-guided algorithms could improve outcomes, though further validation studies are needed.

Limitations

We acknowledge several limitations in our study. This study's retrospective, single-center design may introduce biases and limit generalizability. The relatively small sample size further constrains the applicability of our findings. We recognize that our exclusion criteria may have introduced selection bias, particularly excluding patients with preexisting coagulopathy and those on anticoagulation therapy. While these exclusions were necessary to evaluate SIC specifically attributable to sepsis without confounding factors, they limit our ability to generalize findings to all septic patients, especially those with complex comorbidities. This could potentially lead to an underestimation of the overall coagulopathy burden in the general sepsis population, as patients with baseline coagulation disorders might experience more severe derangements during sepsis. In addition, we did not differentiate between SIC present at sepsis onset and SIC developing later, which could influence its prognostic value. Future prospective, multicenter studies are needed to validate these findings and provide comprehensive insights into SIC in diverse sepsis populations.

Conclusions

The prevalence of SIC is higher in our population than in other cohorts, and a SIC score ≥4 serves as an independent predictor for 28-day mortality. These findings have important clinical implications. First, the SIC score should be utilized as an early prognostic tool to identify high-risk septic patients who may require more aggressive management. Second, early monitoring and targeted intervention strategies for patients with SIC, including more frequent reassessment of coagulation parameters and organ function, may improve treatment outcomes. Third, SIC scoring could potentially guide anticoagulant therapy decisions in septic patients, though specific protocols require further validation. Early detection and management of coagulopathy using the easily calculated SIC score may significantly improve sepsis outcomes, particularly in critical care settings. Further prospective, multicenter studies are needed to clarify SIC's value across different patient populations and healthcare systems.

Author contributions statement

HPQ: Conceptualization (lead); writing – original draft (lead); formal analysis (lead). NHT: writing – original draft (equal); writing – review and editing (equal); formal analysis (equal). NTT: writing – original draft (equal); PDH: Conceptualization (equal); Writing – review and editing (lead); formal analysis (equal).

Conflicts of interest

None Declared.

Ethical approval

Ethics Committee of the 108 Military Central Hospital approved this study with document reference number 2757/GCN – BV on May 10, 2024.

Funding

None.

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